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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/480,389	01/11/2000	Bruce M. Boman	CATX-N	4258
24988	7590	03/18/2005	EXAMINER	
LEONA L. LAUDER 465 CALIFORNIA, SUITE 450 SAN FRANCISCO, CA 94104-1840			HOLLERAN, ANNE L	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 03/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/480,389

Applicant(s)

BOMAN, BRUCE M.

Examiner

Anne Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 18 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 24-28,32-35,37-44,55-57 and 59-72 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 24-28,32-35,37-44,55-57 and 59-72 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 11/18/2004.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. The amendment filed November 18, 2004 is acknowledged. Claims 73-80 were canceled without prejudice.

Claims 24-28, 32-35, 37-44, 55-57 and 59-72 are pending and examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections Withdrawn:***

3. The rejection of claims 24-28, 32-35, 37-39, 43, 44, 55-57, 61, 73-77, 79, and 80 under 35 U.S.C. 103(a) as being unpatentable over Glendening (Glendening, J. M. et al., Cancer Res. 55: 5531-5535, 1995) in view of Nozawa (U.S. Patent 5,328,826; issued July 12, 1994; filed March 23, 1992) is withdrawn in view of the amendment canceling claims 73-80 and in view of applicant's arguments that appear to indicate that Glendening fails to enable a method for detecting a germline mutation of p16INK4 in normal cells by detecting an about 50% decrease in protein levels.

#### ***Claim Rejections Maintained:***

4. The rejection of claims 24-28, 32-35, 37-44, 55-57 and 59-72 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for the reasons of record. New grounds of rejection necessitated by the amendment are presented.

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The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendment introduces new matter because the phrase “wherein said disease or said disease susceptibility trait has been associated with a germline mutation that causes an about 50% decrease in the level of wild-type protein” has no support in the specification as originally filed. The phrase “has been associated” implies a time frame for the “association”. The specification fails to discuss this concept. Is the association as of the current amendment or is the association as of the effective file date of the application?

The claims as currently amended are not fully described by the specification, and therefore, introduce new matter in to the specification, because the scope of the claimed invention is different from the scope of what is described in the passages pointed to by applicant. Applicant points to a passage on page 2, lines 24-27, where the specification teaches that assays of the invention are based on the assumption that gene expression directly relates to gene dosage. However, wherein said disease or said disease susceptibility trait has been associated with a germline mutation that causes an about 50% decrease in the level of wild-type protein” is broader in scope because an “association “ be one that exist because of theoretical assumption, as alluded to in the specification, or because of an empirical finding. Therefore, the amendment introduces new matter into the specification because the phrase “has been associated” is different in scope from the concept presented in the specification of a theoretical association between a heterozygous mutation that may produce an about 50% decrease in a level of a protein.

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5. Claims 24-28, 32-35, 43, 44, 55-57, and 61 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Pece (Pece, N. et al. J. Clin. Invest. 100(10): 2568-2579, 1997, November; cited in IDS) in view of Nozawa (U.S. Patent 5,328,826; issued July 12, 1994; filed March 23, 1992).

Applicant's arguments have been carefully considered, but fail to persuade. Applicant presents arguments by discussing the references separately instead of the rejection as a whole. Applicant asserts that Nozawa is not analogous art because Nozawa teaches quantitation of cancer antigens isolated from cancer cells instead of protein isolated from normal cells, and further because Nozawa is interested in determining a cut-off value for establishing whether an immunological signal represents a detection of a protein and not a false-positive. These arguments are not found persuasive because Nozawa is cited for the purpose of demonstrating that methods for quantitating protein are known in the art and the use of a ratio of a level of a protein of interest to a level of a housekeeping protein is known.

The claimed inventions include within their scope methods where one of the two subject genes is a housekeeping gene, and therefore, read on methods where one of the protein detected is detected for the purpose of ensuring that differences observed in protein levels between different samples is due to an actual difference in protein levels per cell and not due to an experimental artifact such as different loading between samples. This is one of the problems addressed in Nozawa (see col. , line 44-48 and col. 3, lines 18-52). Therefore, Nozawa is analogous art.

With regard to Pece, applicant argues that the ratios cited in Pece are not the same ratios as what is claimed. This not persuasive because applicant teaches in the specification that based

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on a theory that a heterozygous mutation results in loss of protein expression from one allele, one would then expect that the difference between a normal individual and one with the heterozygous mutation would be an observation of about a 50% loss in protein expression. Therefore, one would expect that samples from a normal and a mutated individual would differ in absolute amounts by about 50%. However, the technical step of ensuring that the observed difference is due an actual difference in protein expression and not a difference in protein loading between samples must be done. In the case of Pece, as discussed in the previous Office action, Peces noted an about 50% reduction in protein expression where the expression levels of other genes were also examined and found to be unchanged and used this finding of unchanged levels in the other genes to justify a conclusion that the observation of a 50% reduction was a real reduction and not due to an experimental artifact (page 2573, col. 1). Applicant has failed to provide evidence that Pece's results are invalid or that the findings of Pece fail to demonstrate a heterozygous mutation that produces an about 50% decrease in protein expression. Therefore, the rejection is maintained.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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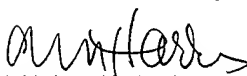
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (571) 272-0833. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 571-1600.

Anne L. Holleran  
Patent Examiner  
March 17, 2005

  
**ALANA M. HARRIS, PH.D.**  
**PRIMARY EXAMINER**  
03/17/2005